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(54) Intron sequence analysis method for detection of adjacent and remote locus alleles as haplotypes.

(57) The present invention provides a method for detection of at least one allele of a genetic locus and can be used to provide direct determination of the haplotype. The method comprises amplifying genomic DNA with a primer pair that spans an intron sequence and defines a DNA sequence in genetic linkage with an allele to be detected. The primer-defined DNA sequence contains a sufficient number of intron sequence nucleotides to characterize the allele. Genomic DNA is amplified to produce an amplified DNA sequence characteristic of the allele. The amplified DNA sequence is analyzed to detect the presence of a genetic variation in the amplified DNA sequence such as a change in the length of the sequence, gain or loss of a restriction site or substitution of a nucleotide. The variation is characteristic of the allele to be detected and can be used to detect remove alleles. Kits comprising one or more of the reagents used in the method are also described.

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## EUROPEAN SEARCH REPORT

Application Number

EP 90 30 9107

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Y	EP-A-0 256 630 (HOWARD HUGHES MEDICAL INSTITUTE) * the whole document * *especially pages 24 and 25.* ---	1-11	C12Q1/68 C07H21/04
Y	EP-A-0 269 260 (BIOTECHNOLOGY RESEARCH PARTNERS LTD.) * abstract * *pages 3-13.* ---	1	
Y	NATURE vol. 322, no. 6082, August 1986, LONDON pages 799 - 803; DILELLA, A. G. ET AL.: 'TIGHT LINKAGE BETWEEN A SPLICING MUTATION AND A SPECIFIC DNA HAPLOID IN PHENYLKETONURIA' * the whole document * ---	1-11	
D, Y	THE LANCET vol. I, March 1988, LONDON pages 497 - 499; DILELLA, A. G. ET AL.: 'SCREENING FOR PHENYLKETONURIA MUTATIONS BY DNA AMPLIFICATIONS WITH THE POLYMERASE CHAIN REACTION' * the whole document * ---	1-11	TECHNICAL FIELDS SEARCHED (Int. Cl.5)  C12Q
Y	WO-A-8 904 875 (CETUS CORPORATION) * the whole document * ---	1-12, 17-34	
P, X	WO-A-8 912 697 (THE BOARD OF REGENTS OF THE UNIVERSITY OF WASHINGTON) * the whole document * ---	1-11	
P, X	EP-A-0 364 255 (BAYLOR COLLEGE OF MEDICINE) * the whole document * ---	1-11	
P, Y	WO-A-8 911 547 (CETUS CORPORATION) * the whole document * ---	1-12, 17-34	
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 29 JUNE 1992	Examiner OSBORNE H. H.
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ..... & : member of the same patent family, corresponding document	

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